DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JUN 10 1993

R. William Soller, Ph.D.
Senior Vice President and
Director of Science & Technology
Nonprescription Drug Manufacturers Association
1150 Connecticut Avenue, NW
Washington, DC 20036

Re: Docket No.78N-036L
Comments No. C144, LET58,
LET54, SUP7

Dear Dr. Soller:

This letter is in response to the Nonprescription Drug Manufacturers Association's (NDMA) submission dated November 23, 1992, concerning your research protocols designed to obtain information on physician and consumer understanding of various terms pertaining to the statement of identity (SOI) of OTC laxative drug products containing fiber. These products are included in the OTC drug review as bulk-forming laxative drug products. Your submission is filed as comment No. C144 under Docket No. 78N-036L in the Dockets Management Branch.

In my letter to you dated July 30, 1992 (LET58), I stated that the two protocols included in your May 1, 1992 (LET54) and June 1, 1992 (SUP7) submissions would not provide sufficient data to support a change in the SOI for bulk-forming laxative drug products. The November 23, 1992 submission contains revisions to these two protocols. You have stated that the revised protocols are designed to determine the attitudes and perceptions of physicians and consumers relating to the following three proposed statements of identity: 1. "Fiber Therapy for Irregularity (regularity was changed to irregularity);" 2. "Bulk-forming Laxative;" and 3. "Fiber Laxative." The revised protocols are also designed to determine consumer and physician perception and understanding of specific warning language in the labeling of fiber-containing OTC drug products. You stated that the agency made no mention of this latter issue in my July 30, 1992 letter.

The Office of OTC Drug Evaluation has reviewed your latest submission and concludes that the protocols will not provide sufficient data to support a change in the statement of identity for bulk-forming laxative drug products to "Fiber therapy for irregularity." We reach this conclusion for the following reasons:

First, the protocols do not address the concerns expressed in my July 30, 1992 letter regarding consumer understanding of "irregularity". In that letter, we questioned whether relief of

occasional constipation and avoidance of irregularity are medically synonymous. For relief or avoidance of "irregularity," long term therapy is suggested. Therefore, unless the clinical studies that support the claim for relief of occasional constipation (short term use) could also be found adequate to support the claim for relief or avoidance of irregularity (long term use), separate clinical trials would be needed to support the irregularity claim. Second, we are not aware of clinical studies that would adequately support a long-term indication.

Even if surveys were to be conducted, the proposed protocols have a number of problems, as discussed below:

1. There is some concern whether the consumer panel will adequately represent "ordinary" consumers. The protocol needs to include a method whereby a "representative" sample of consumers is obtained to participate in the study. Considering what is known about "volunteering biases," people who participate in these panels are not "ordinary".

2. The consumer study protocol does not directly measure what it purports to measure, i.e., consumer understanding of certain terms related to laxatives. The consumer study asks how easy or difficult the selected test terms are to understand, how descriptive the terms are of the products shown, and how much consumers agree or disagree that such products can be described by these terms. The decision regarding the appropriateness of the statement of identity is based on three terms. This narrow list of terms does not provide a test of the "best" possible terms to describe the proper use of the product. No terms will be tested that would more clearly communicate the intended use of these products to consumers nor does the study directly measure if consumers correctly understand the terms. Rather it measures respondents' attitudes about their own understanding of the term. How do consumers know whether or not they "understand" if a phrase is correct or incorrect? There is good research evidence that consumers have little knowledge of how well or poorly they understand a concept. A more direct method to measure consumer understanding would be to ask consumers to "check off" statements that describe how the product should or should not be used. This method may also detect whether different terms connote different usage patterns (e.g., long term vs. short term use).

3. The questions purported to deal with consumer and physician perception and understanding of specific label warning language relate more to consumers' ability to read than on "understanding".

4. The protocols should include, a priori, a set of criteria for interpreting the data. No information is given as to how the data will be analyzed and what criteria will be used to determine if a term or phrase is acceptable or unacceptable, misleading or nonmisleading.

5. The rationale for the physician survey is not clear. How would physicians know if a consumer would understand the terms being tested (question 5 on the physician questionnaire)? The questions in the physician survey will not provide direct information about physicians' views of how consumers would actually use these products. The questions ask physicians if they have any "concerns" about use of the products. Physicians may believe that these products are so safe that there could not be any safety problems, whether or not the products are misused. A more direct set of questions, measuring how products with different statement of identities would be used, would be a better measure of physicians' views.

6. Both the physician and the consumer protocols call for a mail panel. The rationale for the mail panel is not clear, particularly in light of NDMA's comments in a letter to FDA on September 18, 1991 regarding a similar proposed study on consumers' knowledge, attitudes, and beliefs about claims and warnings. In that letter, James Cope of NDMA opposed the use of mail panels. Mr. Cope stated the following:

> "This type of panel consists of those who are willing to participate in testing and they are kept in a data base and utilized for testing of ads, products, concepts, and the like. The recruiting of mail panel consumers is a strenuous one in which only about 4% of the total population agrees to participate."

NDMA further stated in a letter to FDA on April 20, 1992:

> "We [NDMA] propose [that FDA] . . . limit the study to Phase I of the latest protocol, eliminating the

> Phase II mail panel portion. For reasons we discussed on March 26, 1992, we feel the mail panel is an inadequate approach to the issue of compliance with warnings."

7. The protocols do not address how the home setting will affect consumers' responses to the survey questions. The proposed consumer questionnaire specifically asks participants questions about a label that they are reading which has been mailed to them at home. NDMA's September 18, 1991 letter further stated,

> "The assessment of labels in an 'unnatural' setting could be different than taking [the] product either in the home or at a store shelf. The proposed study under FTC 0274-91 is by mail and respondents are at home. There is little control over whom they speak to or what they read. In addition, it could be hypothesized that those who typically have used a product over a long period of time would not be consistently reading the labels. But those who are new to a brand of OTC medicine would in fact take the time to read the warning label. It is not clear that this has been worked into the design."

8. The consumer protocol, but not the physician protocol, included a power analysis. Information is needed on how the sample size of 200 physicians was determined and a description of the power of the sample.

9. We believe that, in a consumer study of level of comprehension and attention to warning labels, a 20% level of imprecision is inappropriate. The level of imprecision should be 10% or less.

Based on the information contained in your submission, the Office of OTC Drug Evaluation concludes that the data generated from implementation of the proposed protocols would not provide sufficient evidence to change the statement of identity of bulk forming laxatives to "Fiber therapy for Irregularity." The term "Fiber therapy for irregularity" implies that the drug corrects, avoids, or prevents irregularity; in our view, such claims would require the submission of clinical studies. Terms such as "Bulk-

forming laxative" or "Fiber laxative" when used as statements of identity would not require such clinical proof because these terms do not imply prevention or long term correction of disease.

Further, certain regulations must be considered in determining the statement of identity. Under the regulations in 21 CFR 201.61, the statement of identity of an OTC drug is limited to the established name of the drug, if any, followed by an accurate statement of the general pharmacological category(ies) of the drug or the principal intended action(s) of the drug. The established name of the drug is defined in section 502(e)(3) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352(e)(3)). The recognized pharmacological category for a drug used to relieve constipation is "laxative." Because of the many classes of laxatives, and for the sake of clarification, a term describing the class to which a particular laxative drug belongs is also included in the monograph. Based on the regulations in 21 CFR 201.61 and the tentative final monograph, an example of a statement of identity for a product containing bran for the relief of constipation would be "bran" followed by the term "bulk forming laxative," i.e., the established name of the drug and its pharmacological category. Wherever possible, the agency prefers to use the general pharmacologic category as the statement of identity because information on the principal intended action is provided in the indications. However, we might consider including the term "fiber laxative" as an optional (allowable) indication for bulk-forming laxatives in the final monograph as follows: "Fiber therapy for relief of occasional constipation" [which may be followed by "(irregularity)"].

Any comment you may wish to make on the above information should be submitted in three copies, identified with the docket and comment numbers shown at the beginning of this letter, to the Dockets Management Branch (HFA-305), Food and Administration, Room 1-23, 12420 Parklawn Drive, Rockville, MD 20857.

We hope this information will be helpful.

Sincerely yours,

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